amplifying a highly conserved region within a human-*P. carinii* nucleic acid sequence, if such sequence is present in the specimen, using two or more oligonucleotide primers that hybridize to the highly conserved region; and

determining whether an amplified sequence is present;

wherein the highly conserved region has at least 79% sequence identity with residues 2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), 2809-3054 of *HMSG33* (SEQ ID NO: 11), or 1-249 of *HMSGp2* (SEQ ID NO: 15); or at least 84% sequence identity with residues 2821-3072 of *HMSG35* (SEQ ID NO: 13).

REMARKS

By this amendment, ten paragraphs of the specification and claims 1, 3-14, 16-18, and 21-24 have been amended, claim 15 has been canceled, and new claims 25-32 have been added. No new matter is introduced by these amendments. Where necessary, support for the language of each amendment and new claim is discussed below. Unless specifically stated otherwise, none of these amendments are intended to limit the scope of any claim.

After entry of this amendment, **claims 1-14 and 16-32 are pending in the application** and considered in a condition for allowance. Consideration of the pending claims is respectfully requested.

Telephone Interview:

Applicants thank Examiner Goldberg for granting their undersigned representative a telephone interview regarding this application on August 22, 2002. Also present at that interview was Dr. Debra Gordon, on behalf of the Applicants. Applicants further thank Examiner Goldberg for her follow up voicemail to their undersigned representative on August 22, 2002, and for the Summary of Interview of the same date.

The rejections of the pending claims under 35 U.S.C. §112, 2nd paragraph and 35 U.S.C. §103 (particularly Garbe *et al.*) were the subject of the telephone interview and the follow-up voicemail. Specific language that might resolve these rejections was discussed in the interview. As described more fully below, certain issues were clarified during the interview and we believe understanding was reached on several issues. On those issues that were not fully resolved during the interview or that were raised in the follow-up voicemail, Applicants believe this amendment reflects suggestions that were made by the Examiner.

Correction of Clerical Errors

During preparation of this response, Applicants became aware of a few clerical errors, which had been carried throughout the application, related to the nucleotide numbers delineating the beginning of the highly conserved regions of HMSGp1 and HMSG33. By this amendment, six paragraphs in the specification, and claims 4, 5, 6, and 7, have been amended to correct these obvious errors. Support for these amendments can be found at least by comparing the first boxed amino acids (in Figure 1L) for HMSGp1 and HMSG33 with the corresponding amino acid and nucleotide sequence in the Sequence Listing at page 5 and 43, respectively.

In addition, Applicants became aware of a clerical error related to the identification of the nucleotides of SEQ ID NO: 11 that correspond to the nucleic acid sequences of SEQ ID NO: 17, SEQ ID NO: 19 and SEQ ID NO: 20. By this amendment, three paragraphs of the specification have been amended to correct the obvious errors. Support for the amendments can be found at least by comparing SEQ ID NO: 17, SEQ ID NO: 19 and SEQ ID NO: 20 in the Sequence Listing as originally filed at pages 55 and 56 with SEQ ID NO: 11 in the Sequence Listing as originally filed at page 43.

Restriction Requirement:

Applicants thank Examiner Goldberg for withdrawing the sequence restriction with respect to the method claims.

Embedded Hyperlinks:

As requested by the Examiner, Applicants have amended the specification at pages 9 and 10 to remove the embedded hyperlinks. Applicants request that the objections to the specification on this ground be withdrawn.

Improper Dependent Form:

Claims 6 and 11-16 have been objected to under 37 C.F.R. § 1.75(c) for failing to further limit the subject matter of the claim from which each originally depended. Claim 15 has been canceled and claims 6, 11-14, and 16 have each been amended to depend from a different claim. Thus, in each case, the objection of the Examiner has been render moot, and Applicants request that the objections to claims 6 and 11-16 on these grounds be withdrawn.

Claims 21 and 22 have been objected to for depending upon one another. Applicants thank Examiner Goldberg for pointing out this inconsistency. Claims 21 and 22 have each been amended to depend from claim 20, which corrects the inconsistency. Applicants request that the objections to claims 21 and 22 on this ground be withdrawn.

Claim rejections under 35 USC §112, 1st paragraph:

Claims 3 and 4 have been rejected under 35 U.S.C §112, 1st paragraph because the concept of "at least 79% sequence identity with residues 2821 – 3072 of HMSG35 (SEQ ID NO: 13)" contained in such claims is allegedly not described in the specification. Applicants traverse this rejection.

Claim 3 has been amended to delete the allegedly undisclosed concept. Further, claim 4 has been amended to depend from claim 1, which does not contain the alleged new matter. Therefore, the rejections of claims 3 and 4 based on 35 U.S.C §112, 1st paragraph are rendered moot and Applicants request that the rejections be withdrawn.

As discussed in more detail below, claim 1 has been amended to clarify that the highly conserved region is a nucleic acid sequence having certain percentage identity to residues in the sequences disclosed by Applicants, including without limitation at least 84% sequence identity

with residues 2821-3072 of *HMSG35* (SEQ ID NO: 13). Applicants' disclosed sequences (described throughout the specification and Sequence Listing) as summarized by the highly conserved region (HCR) Alignment clearly show that the specified residues of HMSG35 are at least 84% identical to other MSG encoding sequences of *human P. carinii*. Thus, amended claims reciting "at least 84% sequence identity with residues 2821-3072 of *HMSG35* (SEQ ID NO: 13)" is properly supported and described in the specification.

Claims 5-7 have been rejected under 35 U.S.C. §112, 1st paragraph because the specification allegedly fails to teach that the highly conserved regions are 91% to 100% identical at the nucleotide level. Applicants traverse this rejection.

With respect to claims 6 and 7, Applicants respectfully disagree with the Examiner. The specification discloses the nucleic acid sequence of the highly conserved regions of the MSG clones (*e.g.*, page 3, lines 6-10 and in the Sequence Listing at pages 5 (SEQ ID NO: 1), 12 and 13 (SEQ ID NO: 3), 20 (SEQ ID NO: 5), 28 (SEQ ID NO: 7), 36 (SEQ ID NO: 9), 43 (SEQ ID NO: 11), 51 (SEQ ID NO: 13), and 55 (SEQ ID NO: 15)). Further, the specification discloses how the ordinarily skilled artisan may align such sequences and determine the percentage sequence identity (*e.g.*, page 9, line 1 through page 10, line 27). Applicants earlier provided to the Examiner in the Response to Restriction Requirement, filed February 9, 2001, the results of an alignment of the nucleic acid sequences of the highly conserved regions (hereafter referred to as the "HCR alignment"). Those results demonstrate that the highly conserved regions of the disclosed MSG clones are 79 - 100% identical at the nucleotide level. The range of "at least 91% identical, namely 91 – 100% identity" as described by the Examiner is contained within the range of identity values determined by direct comparison of the disclosed nucleic acid sequences in the specification. Applicants believe that this language as used in claims 6 and 7 is allowable as fully enabled by the disclosure, and therefore Applicants request that this rejection of claims 6 and 7 be withdrawn.

Claim 5 has been amended to delete the language regarding 91% sequence homology. Therefore, this rejection of claim 5 is now moot.

Claim rejections under 35 USC §112, 2nd paragraph:

Claims 1-22 have been rejected under 35 U.S.C. §112, 2nd paragraph, for allegedly being indefinite for failing to define the term "highly conserved region." This rejection was briefly discussed during the telephone interview. Applicants' representative explained Applicants' intention to clarify claim 1 with respect to the allegedly undefined term. Proposed language was read to the Examiner over the telephone.

Applicants do not concede that the term "highly conserved region" is indefinite. However, to advance prosecution in this case, Applicants have amended claim 1 to add language clarifying the term "highly conserved region" as it is used in the claims. Specifically, the following phrase has been added to claim 1:

> "wherein the highly conserved region has at least 79% sequence identity with residues 2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), 2809-3054 of *HMSG33* (SEQ ID NO: 11), or 1-249 of *HMSGp2* (SEQ ID NO: 15); or at least 84% sequence identity with residues 2821-3072 of *HMSG35* (SEQ ID NO: 13)"

Support for this amendment can be found throughout the specification, for example, at page 3, lines 6-10, or page 13, lines 8-12, together with the HCR alignment (discussed above). Claims 2-22 depend from claim 1 and thus also incorporate the clarification of the term "highly conserved region," which satisfies the definiteness requirement. In light of this amendment, Applicants ask that the Examiner reconsider and withdraw this rejection of claims 1-22.

The Examiner is correct to recognize that the boxed amino acid sequence shown in Figure 1L and described in the figure legend as the "conserved carboxy-terminal region of the proteins" is not identical to the regions delineated elsewhere in the specification as the conserved regions. However, Applicants are not limited to the single embodiment illustrated in Figure 1L. As the Examiner recognizes in the Office Action Summary by citing "page 13," the specification clearly supports the broader conception of a highly conserved region (see specifically, page 13, lines 8-12 or, *e.g.*, page 3, lines 6-10). Thus, Applicants request that this rejection to claims 1-22 be withdrawn.

Claims 1-22 have been rejected under 35 U.S.C. §112, 2nd paragraph, as being allegedly indefinite because the recitation "amplifying a highly conserved region within a human *P. carinii* nucleic acid" does not make clear whether the primers are taken from the human *P. carinii* region or whether the nucleic acid which is contacted with the primers is human P. carinii nucleic acid. During the telephone interview, Examiner Goldberg suggested that describing the source of the biological sample in claim 1 as "human" would satisfy her concern in this regard. Applicants appreciate the Examiner's help in understanding the point of confusion. Claim 1 has been amended to specify a "human biological sample," as suggested by the Examiner. Support for this amendment can be found throughout the specification, for example, at page 26, lines 13-34. Claims 2-22 depend from claim 1 and thus also specify a "human biological sample" to satisfy 35 U.S.C. §112, 2nd paragraph. In light of this amendment, Applicants ask that the Examiner reconsider and withdraw this rejection of claims 1-22.

Claims 1-22 have been rejected under 35 U.S.C. §112, 2nd paragraph, for allegedly being indefinite for failing to define the phrase "derived from." Applicants have amended claim 1 to substitute the phrase "that hybridize to a" for "derived from." The Examiner recognized in claim 23 that hybridization to a human *P. carinii* nucleic acid sequence is sufficiently definite to satisfy 35 U.S.C. §112, 2nd paragraph. Claims 2-22 depend directly from claim 1, and thus also incorporate the substitution of the phrase "that hybridize to a" to satisfy §112.

During the telephone interview, Examiner Goldberg suggested that it would also be desirable to add dependent claims specifying the conditions under which hybridization occurs. In response, the Applicants have amended dependent claims 3 and 8 to specify low stringency (supported for instance at page 15, line 29-30) and stringent hybridization conditions (supported for instance at page 15, line 25-26). In light of these amendments and arguments, Applicants ask that the Examiner reconsider and withdraw this rejection of claims 1-22.

Claims 3-7 have been rejected under 35 U.S.C. §112, 2nd paragraph, for allegedly being indefinite because it is unclear what portions of the identified sequences are being compared to determine the stated percentage sequence identity. Further, as Examiner Goldberg explained

during the telephone interview, it was unclear to her to what sequences the oligonucleotide primers hybridize.

With respect to percentage sequence identity: As discussed previously, Claim 3 has been amended to delete the reference to 79% sequence identity to SEQ ID NO: 13. Claim 4 has been amended to depend from claim 1 instead of from claim 3. Claim 5 has been amended to delete the reference to 91% sequence homology to identified residues. Hence, as amended, none of claims 3, 4 or 5 recite sequences having any percentage sequence identity. Thus, this rejection has been rendered moot with respect to claims 3, 4 and 5. Applicants have amended claims 6 and 7 to recite that percentage homology between the oligonucleotide primer and the stated residues is to be determined by comparison of the primer to "approximately the same number of nucleotides" of the stated residues. It is inherently true that a primer contains a set number of nucleotides and that it can hybridize to approximately the same number of nucleotides of the target sequence. Thus, this amendment is supported by the inherent characteristics of primers and hybridization.

With respect to primer hybridization: Claim 1, from which claims 3-7 now depend, has been amended to state that at least one oligonucleotide primer hybridizes to specified residues of the nucleic acid sequences disclosed by Applicants. This amendment is supported by the description of such sequences found throughout the specification and in the Sequence Listing.

Based on these amendments and arguments, Applicants request that the rejection of claims 3-7 on these grounds be withdrawn.

Claims 9 and 10 have been rejected under 35 U.S.C. §112, 2nd paragraph, for allegedly being indefinite for failing to define the relationship between "upstream" and "downstream" primers. This rejection was discussed with Examiner Goldberg during the telephone interview. The Examiner agreed that the allegedly indefinite terminology is common parlance in the art and that the rejection would be reconsidered. Therefore, Applicants ask that the Examiner withdraw this rejection of claims 9 and 10.

Claims 21 and 22 have been rejected under 35 U.S.C. §112, 2nd paragraph, for allegedly being indefinite because each claim depends upon the other. Claims 21 and 22 have each been amended to depend from claim 20. Applicants request that the rejection of claims 21 and 22 on this ground be withdrawn.

Claims 23 and 24 have been rejected under 35 U.S.C. §112, 2nd paragraph, for allegedly being indefinite for failing to define the phrase "derived from." Claim 23 has been amended to delete the allegedly indefinite phrase. Claims 24 depends directly from claim 23, and thus claim 24 also no longer incorporates this phrase. In light of this amendment, Applicants ask that the Examiner reconsider and withdraw this rejection of claims 23 and 24.

Claim 24 has been rejected under 35 U.S.C. §112, 2nd paragraph, for allegedly being indefinite because the recitation "the labeled probe" lacks the proper antecedent basis. Claim 24 has been amended to recite only a probe, which has proper antecedent basis in claim 23. Withdrawal of this rejection of claim 24 is requested.

Claims 22 and 24 have been rejected under 35 U.S.C. §112, 2nd paragraph, for allegedly being indefinite because the recitation "according to" is unclear. As suggested by the Examiner, claims 22 and 24 have been amended to delete the phrase "a nucleic acid sequence according to." Applicants thank the Examiner for the suggested revision and request withdrawal of the rejection of claims 22 and 24 under 35 U.S.C. §112.

Claim rejections under 35 USC §102:

Claims 1, 2, 17, 19, 20 and 23 have been rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Wright *et al.*, *Gene*, 167(1-2): 185-189, 1995 ("Wright"). Wright teaches a single 306 base pair fragment of a gene encoding a human *P. carinii* MSG.

Applicants have amended claim 1 (and, thus, all claims that depend from claim 1) to clearly indicate that the highly conserved region has at least 79% sequence identity with residues 2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32*

(SEQ ID NO: 9), 2809-3054 of *HMSG33* (SEQ ID NO: 11) and 1-249 of *HMSGp2* (SEQ ID NO: 15), or at least 84% sequence identity with residues 2821-3072 of *HMSG35* (SEQ ID NO: 13). Support for this amendment has been provided above.

No significant similarity was found by alignment of the Wright nucleotide sequence with the highly conserved region now referred to in claim 1. Therefore, Wright clearly does not disclose the specified highly conserved region. Because Wright does not teach this element of the subject claims, it cannot provide the basis for their rejection under 35 U.S.C. §102(b). Withdrawal of the rejection under 35 U.S.C. §102 of claims 1, 2, 17, 19 and 20 is requested.

Claim 23 has been amended to specify that the relevant human-*P. carinii* nucleic acid sequence is *HMSGp1* (SEQ ID NO: 1), *HMSGp3* (SEQ ID NO: 3), *HMSG11* (SEQ ID NO: 5), *HMSG14* (SEQ ID NO: 7), *HMSG32* (SEQ ID NO: 9), *HMSG33* (SEQ ID NO: 11), *HMSG35* (SEQ ID NO: 13), or *HMSGp2* (SEQ ID NO: 15). These sequences are disclosed in Applicants' application and are not disclosed by Wright. Therefore, Wright clearly does not and can not teach such sequences, and it therefore can not provide the basis for a rejection of claim 23 under 35 U.S.C. §102(b). Withdrawal of the rejection of claim 23 under 35 U.S.C. §102 is also requested.

Claim rejections under 35 USC §103(a):

Applicants thank the Examiner for pointing out Applicants' obligation under 37 C.F.R §1.56.

Claims 1, 2, 17, 19 and 23 have been rejected under 35 U.S.C. §103(a) as allegedly being obvious in light of Stringer *et al., J. Eukaryot. Microbiol.*, 40: 821-826, 1993 ("Stringer"), in view of Hogan (U.S. Pat. No. 5,595,874, issued January 21, 1997) ("Hogan"). The Examiner specified at page 11, lines 7-8 of the Office Action Summary that this rejection is drawn to claims that do not require any specific region of the MSG encoding sequences. As discussed previously, claims 1 and 23 have been amended to recite specific nucleic acid sequences. Therefore, Applicants request that the rejection of claims 1, 2, 17, 19 and 23 on this ground be withdrawn.

Claims 1-11, 13, 14, 18-20, 23 and 24 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Garbe *et al.*, *Infection and Immunity*, 62(8): 3092-3101, 1994 ("Garbe"), in view of Hogan.

Applicants thank Examiner Goldberg for discussing this rejection thoroughly with their representatives during the telephone conference. Applicants have amended the rejected claims in light of that conversation and in accordance with suggestions made by the Examiner.

As discussed previously, claims 1 and 23 (and therefore claims 2-11, 13, 14, 18-20 and 24, which depend from either claim 1 or claim 23) have been amended to recite a specific highly conserved region within a human-*P. carinii* nucleic acid sequence not taught or suggested by Garbe or Hogan. A prima facie case of obviousness requires that each and every element of the claim be taught or suggested by the prior art reference(s) relied on by the Examiner. Because the references cited by the Examiner in this rejection do not teach or suggest all limitations of the amended claims, such references can not serve as the basis for a rejection of the claims under 35 U.S.C. §103(a). Therefore, Applicants request that the rejection of claims 1-11, 13, 14, 18-20, 23 and 24 on this ground be withdrawn.

Claims 15 and 16 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Garbe in view of Hogan and further in view of Mullis *et al.* (U.S. Pat. No. 4,683,195, issued July 28, 1987) ("Mullis").

The above discussion regarding the §103(a) rejection of claims 1-11, 13, 14, 18-20, 23 and 24 applies with equal force to this rejection of claims 15 and 16, because Garbe does not disclose the specific sequences referred to in independent claim 1. This deficiency is not remedied by either Hogan or Mullis. Therefore, Applicants request that the rejection of claims 15 and 16 on this ground be withdrawn.

Claim 18 has been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Wright or Stringer in view of Hogan and further in view of Chary-Reddy *et al., J. Clin. Microb.* 34(7): 1660-1665, 1996 ("Chary-Reddy").

As discussed above, neither Wright nor Stringer teach or suggest the highly conserved nucleic acid region recited in claim 18. Further, Chary-Reddy does not make up this deficiency. Because the references cited by the Examiner do not teach or suggest the highly conserved nucleic acid region of the claim, none of such references individually or in combination can serve as a proper basis of a §103(a) rejection of claim 18. Applicants therefore request that the rejection of claim 18 on this ground be withdrawn.

Other Changes to the Claims:

In addition to claim amendments discussed above, the claims have also been amended and new claims added as follows:

Claims 1, 9, 17, 18, 21 and 23 have been amended to correct typographical errors related to antecedent basis. These amendments are supported by antecedent language in the amended claim itself or in a claim from which the amended claim depends.

Claims 4, 6-9, 11-14 and 16 have been amended to change claim dependency.

Claims 5, 6, 7, 10 have been amended in form only to remove Markush language or to eliminate unnecessary verbiage.

For clarity, claims 5-7 have been amended to restate the residues recited in claim 1 from which claims 5-7 depend. Support for these amendments has been discussed in connection with claim 1 amendments.

Claim 6 has been amended to specify "91%" sequence homology. Support for this amendment can be found in original claim 5.

Claim 23 has been amended to add hybridization stringency conditions. This amendment is in keeping with Examiner Goldberg's suggestion in connection with 35 U.S.C. §112, 2nd paragraph rejections of claims 1-22. Support for the amendment is found at page 15, line 25-26 of the specification.

Claim 25 has been added. Support for this new claim is found in the specification, for example, at page 3, line 26-27.

Claim 26 has been added. Support for this new claim is found in original claim 5.

Claim 27 has been added. Support for this new claim is found in original claim 7.

Claim 28 has been added. Support for this new claim is found in original claim 5.

Claim 29 has been added. This new claim is supported by the description of the sequences found throughout the specification (see, *e.g.*, SEQ ID NO: 1, .SEQ ID NO: 3, SEQ ID NO: 5, .SEQ ID NO: 7, .SEQ ID NO: 9, .SEQ ID NO: 11, .SEQ ID NO: 13, and SEQ ID NO: 15, respectively beginning at pages 1, 9, 16, 24, 32, 39, 47 and 54 in the Sequence Listing).

Claim 30 has been added. Support for this new claim is found at page 15, line 29-30 of the specification.

Claim 31 has been added. Support for this new claim is found at page 15, line 25-26 of the specification.

Claim 32 has been added. Support for this new claim is found, in part, in original claim 1 and, in remaining part, throughout the specification, for example, at page 3, lines 6-10, together with the results of the HCR alignment, which is discussed in detail previously.

It is believed that all of new claims 25-32 fully satisfy the requirements of patentability.

CONCLUSION

It is respectfully submitted that the present claims are in condition for allowance. If it may further issuance of these claims, the Examiner is invited to call the undersigned patent attorney at the telephone number listed below.

Respectfully submitted,
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Marked-up Version of Amended Claims and Specification
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)

In the Specification:

At page 2, line 37 through page 3, line 13:

This invention encompasses the purified novel human-*P. carinii* proteins represented by SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, and SEQ ID NO: 14, and isolated nucleic acid molecules that encode these proteins. Specific nucleic acid molecules encompassed in this invention include those represented in SEQ ID NO: 1; SEQ ID NO: 2; SEQ ID NO: 3; SEQ ID NO: 4, SEQ ID NO: 5; SEQ ID NO: 6, SEQ ID NO: 7; SEQ ID NO: 15; and SEQ ID NO: 17. Also encompassed within this invention are the isolated nucleic acid sequences that encode the carboxy-terminal conserved about 100 amino acids of the disclosed human-*P. carinii MSG*s; these may be used for amplification or as probes. The sequences of these conserved nucleic acid molecule regions include residues ~~2894~~2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), ~~2887~~2809-3054 of *HMSG33* (SEQ ID NO: 11), 2821-3072 of *HMSG35* (SEQ ID NO: 13), or 1-249 of *HMSGp2* (SEQ ID NO: 15). In addition, this invention encompasses sequences with at least 70% sequence identity to these regions, and recombinant vectors comprising such nucleic acid molecules and conserved regions from within such nucleic acid molecules, as well as transgenic cells including such a recombinant vector.

At page 3, lines 14-31:

Another aspect of this invention provides a method of detecting the presence of *Pneumocystis carinii* in a biological specimen, by amplifying with a nucleic acid amplification method (*e.g.*, the polymerase chain reaction) a human-*P. carinii* nucleic acid sequence using two or more oligonucleotide primers derived from a human-*P. carinii* MSG protein encoding sequence, then determining whether an amplified sequence is present. In a preferred embodiment of this invention, the human-*P. carinii* nucleic acid sequence is a highly conserved region within an MSG-protein encoding sequence. Such a highly conserved region may, for

instance, include residues ~~2894~~2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), ~~2887~~2809-3054 of *HMSG33* (SEQ ID NO: 11), 2821-3072 of *HMSG35* (SEQ ID NO: 13), or 1-249 of *HMSGp2* (SEQ ID NO: 15). A further aspect of this invention is the method of detecting the presence of *Pneumocystis carinii* in a biological specimen, by determining whether an amplified sequence is present, for instance by electrophoresis and staining of the amplified sequence, or hybridization to a labeled probe of the amplified sequence. Appropriate labels for the hybridization probe include a fluorescent molecule, a chemiluminescent molecule, an enzyme, a co-factor, an enzyme substrate, or a hapten. The nucleotide sequence of such a probe can be chosen from any *MSG* gene sequence that is amplified in the detection method, and for instance can include a nucleic acid sequence according to SEQ ID NO: 19.

At page 8, lines 28-33:

Further nucleic acid molecules might comprise at least 15 consecutive nucleotides of the regions encoding the conserved carboxy-terminal portion of each human-*P. carinii MSG* gene. These regions comprise nucleotides ~~2894~~2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), ~~2887~~2809-3054 of *HMSG33* (SEQ ID NO: 11), 2821-3072 of *HMSG35* (SEQ ID NO: 13), and 1-249 of *HMSGp2* (SEQ ID NO: 15), respectively.

At page 9, lines 22-32:

The NCBI Basic Local Alignment Search Tool (BLAST) (Altschul *et al.* (1990) *J. Mol. Biol.* **215**:403-410) is available from several sources, including the National Center for Biotechnology Information (NCBI, Bethesda, MD) and on the Internet, for use in connection with the sequence analysis programs blastp, blastn, blastx, tblastn and tblastx. It can be accessed at ~~http//www.ncbi.nlm.nih.gov/BLAST/~~the NCBI online site under the "BLAST" heading. A description of how to determine sequence identity using this program is available at ~~http://www.ncbi.nlm.nih.gov/BLAST/blast_help.html~~the NCBI online site under the "BLAST" heading and "BLAST overview" subheading. For comparisons of amino acid sequences of

greater than about 30 amino acids, the Blast 2 sequences function is employed using the default BLOSUM62 matrix set to default parameters, (gap existence cost of 11, and a per residue gap cost of 1). When aligning short peptides (fewer than around 30 amino acids), the alignment should be performed using the Blast 2 sequences function, employing the PAM30 matrix set to default parameters (open gap 9, extension gap 1 penalties).

At page 9, line 33 through page 10, line 6

Other members of the gene family of the disclosed human-*P. carinii* MSG proteins typically possess at least 60% sequence identity counted over full-length alignment with the amino acid sequence of human-*P. carinii* MSG using the NCBI Blast 2.0, gapped blastp set to default parameters. Sequence identity over the about 100 C-terminal amino acids will typically be higher than 60%, for instances about 63%. Proteins with even greater similarity to the reference sequence will show increasing percentage identities when assessed by this method, such as at least 70%, at least 75%, at least 80%, at least 90%, at least 95%, or at least 98% sequence identity. When less than the entire sequence is being compared for sequence identity, homologs will typically possess at least 75% sequence identity over short windows of 10-20 amino acids, and may possess sequence identities of at least 85% or at least 90% or 95% depending on their similarity to the reference sequence. Methods for determining sequence identity over such short windows are described at ~~http://www.ncbi.nlm.nih.gov/BLAST/blast_FAQs.html.~~the NCBI online site under the "BLAST" heading and "Frequently Asked Questions" subheading.

At page 12, line 35, through page 13, line 12:

Oligonucleotides that are derived from the human-*P. carinii HMSGp1*, *HMSGp3*, *HMSG11*, *HMSG14*, *HMSG32*, *HMSG33*, and *HMSG35* gene sequences (SEQ ID NOS: 1, 3, 5, 7, 9, 11, and 13, respectively), as well as the fragment of *HMSGp2* disclosed (SEQ ID NO: 15), are encompassed within the scope of the present invention. Preferably, such oligonucleotide primers will comprise a sequence of at least 15-20 consecutive nucleotides of the relevant human-*P. carinii MSG* gene sequence. To enhance amplification specificity, oligonucleotide primers comprising at least 25, 30, 35, 40, 45 or 50 consecutive nucleotides of these sequences may also be used. These primers for instance may be obtained from any region of the disclosed

sequences. By way of example, human-*P. carinii MSG* gene sequences may be apportioned into halves or quarters based on sequence length, and the isolated nucleic acid molecules may be derived from the first or second halves of the molecules, or any of the four quarters. In addition, primers may be specifically chosen from the conserved carboxy-terminal region of each *MSG* coding sequence. This region comprises nucleic acid residues ~~2894~~2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), ~~2887~~2809-3054 of *HMSG33* (SEQ ID NO: 11), 2821-3072 of *HMSG35* (SEQ ID NO: 13), and 1-249 of *HMSGp2* (SEQ ID NO: 15).

At page 17, line 34, though page 18, line 6:

The selection of PCR primers will be made according to the portions of the gene sequence that are to be amplified. For use in PCR detection of *P. carinii*, it is advantageous to choose primer-annealing sites that are highly conserved across many different members of the human-*P. carinii MSG* gene family. For instance, it is advantageous to choose primer sites from within the regions of human-*P. carinii* sequence displaying greater than 63% sequence identity across the disclosed family members, *e.g.*, that portion of the gene encoding the conserved carboxy-terminal region of the protein. The highly conserved carboxy-terminal regions of the disclosed genes are as follows: residues ~~2894~~2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), ~~2887~~2809-3054 of *HMSG33* (SEQ ID NO: 11), 2821-3072 of *HMSG35* (SEQ ID NO: 13), and 1-249 of *HMSGp2* (SEQ ID NO: 15).

At page 18, lines 20-32:

The presence of amplified human-*P. carinii MSG* sequences can be determined in any conventional manner, including electrophoresis and staining (for instance, with ethidium bromide) of the amplified sequence, or hybridization of a labeled probe to the amplified sequence. For general guidelines on such techniques, see *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor, New York (1989), and *Current Protocols in Molecular Biology*, Greene Publishing Associates and Wiley-Intersciences (1987). Hybridization probes appropriate

for use in detection of amplified human-*P. carinii MSG* sequences are essentially equivalent to those described above for direct hybridization. The region of the gene that has been amplified will be important in choosing an appropriate probe; the detection probe should hybridize to a sequence that falls between the ends of the amplification primers such that the annealing site of the probe is amplified. By way of example, one appropriate oligonucleotide probe is JKK16 (SEQ ID NO: 19), which corresponds to residues of ~~3004~~2926-~~3029~~-2950 of *HMSG33*. This probe could be used for detection of both full-length and carboxy-terminal amplified fragments of human-*P. carinii MSG* genes.

At page 27, lines5-12:

***MSG* sequence:** For PCR amplification of human-*P. carinii MSG* in clinical samples, the upstream primer used was an equimolar mixture of JKK14 (SEQ ID NO: 17) (corresponding to the residues of ~~2887~~2809-~~2911~~-2833 of *HMSG33,* which is also 2845-2869 of *hMSG11*) and JKK15 (SEQ ID NO: 18) (corresponding to the residues of 2836-2860 of *HMSG32*). The downstream primer used was JKK17 (SEQ ID NO: 20) (complementary to the conserved residues ~~3106~~3028-~~3130~~-3052 of *HMSG33,* which is also 3064-3088 of *MSG11*). In experiments wherein the amplified product was detected using the DELFIA™ system, the downstream primer was biotinylated at the 5' end to allow specific capture of amplified sequences through the use of streptavidin.

At page 28, lines 3-13

Southern Blotting: Standard southern blotting techniques were used to confirm the PCR results (Tables 2 and 3). Following agarose gel electrophoresis, PCR products were transferred to Hybond N+ membranes (Amersham, Live Science, Arlington Heights, IL). Amplification of human-*P. carinii MSG* was detected using probe JKK16 (SEQ ID NO: 19), which corresponds to residues of ~~3004~~2926-~~3029~~-2950 of *HMSG33*. Amplification of *P. carinii* MRSU was detected using pAZ102-L2 (Wakefield *et al.* (1990) *Mol. and Biochem. Parasitol.* 43:69-76). Oligonucleotides were labeled with [γ-^{32}P]-ATP by T4 polynucleotide kinase (Ready-to-Go™ Molecular Biology Reagents, Pharmacia Biotech, Denmark). Prehybridization and hybridization were performed overnight at 52° C in 6 X SSPE, 1% sodium dodecyl sulfate (SDS), 10 X

Denhardts' solution (Research Genetics, Huntsville, Alabama). Filters were washed at 52° C in 1 x SSPE, 0.5% SDS for 30 min, then 0.1 x SSPE, 0.5% SDS for 15 minutes.

In the Claims:

1. (**amended**) A method of detecting the presence of *Pneumocystis carinii* in a human biological specimen, comprising:

amplifying a highly conserved region within a human-*P. carinii* nucleic acid sequence, if such sequence is present in the specimen~~sample~~, using two or more oligonucleotide primers ~~derived from~~that hybridize to the highly conserved region ~~human *P. carinii* MSG protein encoding sequence~~; and

determining whether an amplified sequence is present~~.~~;

wherein the highly conserved region has at least 79% sequence identity with residues 2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), 2809-3054 of *HMSG33* (SEQ ID NO: 11), or 1-249 of *HMSGp2* (SEQ ID NO: 15); or at least 84% sequence identity with residues 2821-3072 of *HMSG35* (SEQ ID NO: 13); and

wherein at least one oligonucleotide primer hybridizes to residues 2794-2886 of *HMSGp1* (SEQ ID NO: 1), 2758-2850 of *HMSGp3* (SEQ ID NO: 3), 2845-2937 of *HMSG11* (SEQ ID NO: 5), 2839-2931 of *HMSG14* (SEQ ID NO: 7), 2836-2928 of *HMSG32* (SEQ ID NO: 9), 2809-2901 of *HMSG33* (SEQ ID NO: 11), 2821-2913 of *HMSG35* (SEQ ID NO: 13), or 1-93 of *HMSGp2* (SEQ ID NO: 15).

2. (**reiterated**) The method according to claim 1, wherein amplification of the human-*P. carinii* nucleic acid sequence is by polymerase chain reaction.

3. (**twice amended**) The method of claim 1, wherein the oligonucleotide primers hybridize under low stringency conditions comprising 50°C in 6x SSC, 5x Denhardt's solution, 0.5% SDS and 100 µg sheared salmon testes DNA~~human *P. carinii* nucleic acid sequence is a~~

~~highly conserved region within an MSG protein encoding sequence, wherein the highly conserved region has at least 79% sequence identity with residues 2821-3072 of *HMSG35* (SEQ ID NO: 13)~~.

4. (**twice amended**) The method of claim ~~3~~1, wherein the highly conserved region comprises a sequence selected from the group consisting of: residues ~~2894~~2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), ~~2887~~2809-3054 of *HMSG33* (SEQ ID NO: 11), 2821-3072 of *HMSG35* (SEQ ID NO: 13), and 1-249 of *HMSGp2* (SEQ ID NO: 15).

5. (**twice amended**) The method of claim 1, wherein at least one oligonucleotide primer comprises at least 15 contiguous nucleotides from ~~a sequence chosen from the group consisting of:~~ residues ~~2894~~2794-~~3042~~2886 of *HMSGp1* (SEQ ID NO: 1), 2758-~~3006~~2850 of *HMSGp3* (SEQ ID NO: 3), 2845-~~3090~~2937 of *HMSG11* (SEQ ID NO: 5), 283~~9~~ ~~3084~~2931 of *HMSG14* (SEQ ID NO: 7), 2836-~~3081~~2928 of *HMSG32* (SEQ ID NO: 9), ~~2887~~2809-~~3054~~2901 of *HMSG33* (SEQ ID NO: 11), 2821-~~3072~~2913 of *HMSG35* (SEQ ID NO: 13), ~~and~~ or 1-~~249~~93 of *HMSGp2* (SEQ ID NO: 15)~~ and nucleic acid sequences having at least 91% sequence homology with residues 2894-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), 2887-3054 of *HMSG33* (SEQ ID NO: 11), 2821-3072 of *HMSG35* (SEQ ID NO: 13), and 1-249 of *HMSGp2* (SEQ ID NO: 15)~~.

6. (**twice amended**) The method of claim ~~5~~1, wherein at least one oligonucleotide primer comprises at least 15 contiguous nucleotides ~~from a nucleic acid sequence~~ having at least ~~90~~91% sequence homology with approximately the same number of nucleotides of residues ~~2894~~2794-~~3042~~2886 of *HMSGp1* (SEQ ID NO: 1), 2758-~~3006~~2850 of *HMSGp3* (SEQ ID NO: 3), 2845-~~3090~~2937 of *HMSG11* (SEQ ID NO: 5), 2839-~~3084~~2931 of *HMSG14* (SEQ ID NO: 7), 2836-~~3081~~2928 of *HMSG32* (SEQ ID NO: 9), ~~2887~~2809-~~3054~~2901 of *HMSG33* (SEQ ID NO: 11), 2821-~~3072~~2913 of *HMSG35* (SEQ ID NO: 13), ~~and~~ or 1-~~249~~93 of *HMSGp2* (SEQ ID NO: 15).

7. (**twice amended**) The method of claim ~~5~~1, wherein at least one oligonucleotide primer comprises at least 15 contiguous nucleotides ~~from a nucleic acid sequence~~ having at least 95% sequence homology with approximately the same number of nucleotides of residues ~~2894~~2794 ~~3042~~ 2886 of *HMSGp1* (SEQ ID NO: 1), 2758 ~~3006~~ 2850 of *HMSGp3* (SEQ ID NO: 3), 2845 ~~3090~~ 2937 of *HMSG11* (SEQ ID NO: 5), 2839 ~~3084~~ 2931 of *HMSG14* (SEQ ID NO: 7), 2836 ~~3081~~ 2928 of *HMSG32* (SEQ ID NO: 9), ~~2887~~2809 ~~3054~~ 2901 of *HMSG33* (SEQ ID NO: 11), 2821 ~~3072~~ 2913 of *HMSG35* (SEQ ID NO: 13), ~~and~~ or 1 ~~249~~ 93 of *HMSGp2* (SEQ ID NO: 15).

8. (**amended**) The method of claim ~~5~~1, wherein the oligonucleotide primers hybridize under stringent conditions comprising 65°C in 6x SSC, 5x Denhardt's solution, 0.5% SDS and 100 µg sheared salmon testes DNA~~are chosen from the group consisting of: SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 23, and SEQ ID NO: 24~~.

9. (**amended**) The method of claim ~~5~~1, wherein the ~~pair of~~ oligonucleotide primers consist of one upstream primer and one downstream primer.

10. (**amended**) The method of claim 9, wherein:

the upstream primer is ~~chosen from the group consisting of:~~ SEQ ID NO: 17, or SEQ ID NO: 18~~, SEQ ID NO: 19, SEQ ID NO: 23~~; and

the downstream primer is ~~chosen from the group consisting of:~~ SEQ ID NO: 20 ~~and~~ or SEQ ID NO: 24.

11. (**amended**) The method of claim ~~8~~1, wherein one of the oligonucleotide primers comprises SEQ ID NO: 17.

12. (**amended**) The method of claim ~~8~~1, wherein one of the oligonucleotide primers comprises SEQ ID NO: 18.

13. (**amended**) The method of claim ~~8~~1, wherein one of the oligonucleotide primers comprises SEQ ID NO: 19.

14. (**amended**) The method of claim ~~8~~1, wherein one of the oligonucleotide primers comprises SEQ ID NO: 20.

15. (**canceled**) ~~The method of claim 8, wherein one of the oligonucleotide primers comprises SEQ ID NO: 23~~.

16. (**amended**) The method of claim ~~8~~1, wherein one of the oligonucleotide primers comprises SEQ ID NO: 24.

17. (**amended**) The method of claim 1, wherein the ~~biological~~ specimen is from the oropharyngeal tract.

18. (**amended**) The method of claim 1, wherein the ~~biological~~ specimen is from blood.

19. (**reiterated**) The method of claim 1, wherein the step of determining whether an amplified sequence is present comprises one or more of:

(a) electrophoresis and staining of the amplified sequence; or

(b) hybridization to a labeled probe of the amplified sequence.

20. (**reiterated**) The method of claim 19, wherein the amplified sequence is detected by hybridization to a labeled probe.

21. (**amended**) The method of claim ~~22~~20, wherein the labeled probe comprises a detectable non-isotopic label chosen from the group consisting of:

a fluorescent molecule;

a chemiluminescent molecule;

an enzyme;

a co-factor;

an enzyme substrate; and

a hapten.

22. (**amended**) The method of claim ~~21~~20, wherein the labeled probe comprises ~~a nucleic acid sequence according to~~ SEQ ID NO: 19.

23. (**amended**) A method of detecting the presence of *Pneumocystis carinii* in a human biological specimen, comprising:

exposing the ~~biological~~ specimen to a probe that hybridizes under stringent conditions to a human-*P. carinii* nucleic acid sequence, if the sequence is present in the specimen~~sample~~, to form a hybridization complex; and

determining whether the hybridization complex is present,

wherein the human-*P. carinii* nucleic acid sequence ~~derived from human *P. carinii* is an MSG encoding sequence~~is *HMSGp1* (SEQ ID NO: 1), *HMSGp3* (SEQ ID NO: 3), *HMSG11* (SEQ ID NO: 5), *HMSG14* (SEQ ID NO: 7), *HMSG32* (SEQ ID NO: 9), *HMSG33* (SEQ ID NO: 11), *HMSG35* (SEQ ID NO: 13), or *HMSGp2* (SEQ ID NO: 15); and

wherein the stringent conditions of hybridization comprise 65°C in 6x SSC, 5x Denhardt's solution, 0.5% SDS and 100 µg sheared salmon testes DNA.

24. (**amended**) The method of claim 23, wherein the ~~labeled~~ probe comprises ~~a nucleic acid sequence according to~~ SEQ ID NO: 19.

25. (**new**) The method of claim 23, wherein the probe is a labeled probe.

26. (**new**) The method of claim 1, wherein two or more of the oligonucleotide primers each comprise at least 15 contiguous nucleotides having at least 91% sequence homology with approximately the same number of nucleotides of residues 2794-2886 of *HMSGp1* (SEQ ID NO: 1), 2758-2850 of *HMSGp3* (SEQ ID NO: 3), 2845-2937 of *HMSG11* (SEQ ID NO: 5), 2839-2931 of *HMSG14* (SEQ ID NO: 7), 2836-2928 of *HMSG32* (SEQ ID NO: 9), 2809-2901 of

HMSG33 (SEQ ID NO: 11), 2821-2913 of *HMSG35* (SEQ ID NO: 13), or 1-93 of *HMSGp2* (SEQ ID NO: 15).

27. (**new**) The method of claim 1, wherein two or more of the oligonucleotide primers each comprise at least 15 contiguous nucleotides having at least 95% sequence homology with approximately the same number of nucleotides of residues 2794-2886 of *HMSGp1* (SEQ ID NO: 1), 2758-2850 of *HMSGp3* (SEQ ID NO: 3), 2845-2937 of *HMSG11* (SEQ ID NO: 5), 2839-2931 of *HMSG14* (SEQ ID NO: 7), 2836-2928 of *HMSG32* (SEQ ID NO: 9), 2809-2901 of *HMSG33* (SEQ ID NO: 11), 2821-2913 of *HMSG35* (SEQ ID NO: 13), or 1-93 of *HMSGp2* (SEQ ID NO: 15).

28. (**new**) The method of claim 1, wherein two or more oligonucleotide primers each comprise at least 15 contiguous nucleotides from residues 2794-2886 of *HMSGp1* (SEQ ID NO: 1), 2758-2850 of *HMSGp3* (SEQ ID NO: 3), 2845-2937 of *HMSG11* (SEQ ID NO: 5), 2839-2931 of *HMSG14* (SEQ ID NO: 7), 2836-2928 of *HMSG32* (SEQ ID NO: 9), 2809-2901 of *HMSG33* (SEQ ID NO: 11), 2821-2913 of *HMSG35* (SEQ ID NO: 13), or 1-93 of *HMSGp2* (SEQ ID NO: 15).

29. (**new**) The method of claim 4, wherein two or more of the oligonucleotide primers hybridize to residues 2794-2886 of *HMSGp1* (SEQ ID NO: 1), 2758-2850 of *HMSGp3* (SEQ ID NO: 3), 2845-2937 of *HMSG11* (SEQ ID NO: 5), 2839-2931 of *HMSG14* (SEQ ID NO: 7), 2836-2928 of *HMSG32* (SEQ ID NO: 9), 2809-2901 of *HMSG33* (SEQ ID NO: 11), 2821-2913 of *HMSG35* (SEQ ID NO: 13), or 1-93 of *HMSGp2* (SEQ ID NO: 15).

30. (**new**) The method of claim 29, wherein the oligonucleotide primers hybridize under low stringency conditions comprising 50°C in 6x SSC, 5x Denhardt's solution, 0.5% SDS and 100 µg sheared salmon testes DNA.

31. (**new**) The method of claim 29, wherein the oligonucleotide primers hybridize under stringent conditions comprising 65°C in 6x SSC, 5x Denhardt's solution, 0.5% SDS and 100 µg sheared salmon testes DNA.

32. (**new**) A method of detecting the presence of *Pneumocystis carinii* in a human biological specimen, comprising:

amplifying a highly conserved region within a human-*P. carinii* nucleic acid sequence, if such sequence is present in the specimen, using two or more oligonucleotide primers that hybridize to the highly conserved region; and

determining whether an amplified sequence is present;

wherein the highly conserved region has at least 79% sequence identity with residues 2794-3042 of *HMSGp1* (SEQ ID NO: 1), 2758-3006 of *HMSGp3* (SEQ ID NO: 3), 2845-3090 of *HMSG11* (SEQ ID NO: 5), 2839-3084 of *HMSG14* (SEQ ID NO: 7), 2836-3081 of *HMSG32* (SEQ ID NO: 9), 2809-3054 of *HMSG33* (SEQ ID NO: 11), or 1-249 of *HMSGp2* (SEQ ID NO: 15); or at least 84% sequence identity with residues 2821-3072 of *HMSG35* (SEQ ID NO: 13).